Remarks

Claims 1-18 and 27-44 are pending in the application.

Claims 19-26, and 45-59 have been canceled without prejudice because they are drawn to non-elected inventions. The Applicants expressly reserve the right to prosecute the canceled claims in one or more divisional applications claiming the benefit of priority to the instant application and its predecessor(s). 35 USC § 121.

Claims 1-18 and 27-44 have been amended. Support for the amendments can be found throughout the application, including the claims as originally filed. Therefore, no new matter has been added. Importantly, the claim amendments should not be construed to be an acquiescence to any of the claim rejections. Rather, the amendments to the claims are being made solely to expedite the prosecution of the above-identified application. The Applicants expressly reserve the right to further prosecute the same or similar claims in subsequent patent applications claiming the benefit of priority to the instant application. 35 USC § 120.

Election -- Restriction

The Applicants gratefully acknowledge the Examiner's decision to examine Groups I, II and V in the instant application. To ease prosecution of the expanded set of claims under consideration, the Applicants have canceled without prejudice all claims withdrawn from consideration.

Claim Rejections Based on 35 USC § 112¶2

Claims 1-18 and 27-44 stand rejected under 35 U.S.C. § 112¶2 based on the Examiner's contention that they are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Applicants respectfully traverse this rejection.

A. Claims 1-6 and 27-32 were intended to be directed to compounds, not compositions. The Applicants sincerely apologize for the typographical errors introduced into the preambles of claims 1-4 and 27-30 during preparation of the application. Accordingly, the preambles of claims 1-4 and 27-30 have been amended to replace

"composition" with "compound". Additionally, claims 5-6 and 31-32 have been recast as dependent upon claims 1 and 27, respectively. Importantly, the claim amendments do not reflect a change in the scope of the invention for which protection is sought.

B. Likewise, the Applicants sincerely apologize for the erroneous use of "comprising" in defining Markush groups in the claims. Each instance of this error has been corrected by replacing the forbidden open-ended language with the permitted closed-ended language, e.g., "selected from the group consisting of". Once again, the claim amendments do not reflect a change in the scope of the invention for which protection is sought.

C. The Applicants acknowledge that the term "biomolecule" is indefinite. To expedite prosecution to allowance, the Applicants have amended claims 1, 7, 11, 27, 33, and 37, removing each instance of the term "biomolecule." The Applicants expressly reserve the right to pursue claims to this subject matter in an application claiming the benefit of the filing date of the instant application. 35 USC § 120.

D. Claims 5, 6, 31 and 32 have been reorganized to conform with the requirements of 35 USC 112¶2. All of these claims were intended to be compound claims. Therefore, claims 5 and 6 have been made to depend on claim 1, and claims 31 and 32 have been amended to depend on claim 27. The claim amendments do not reflect a change in the scope of the invention for which protection is sought.

E. Claims 15 and 41 have been reorganized to claim more definitely the method for which protection is sought. This refinement includes the elimination of the terms "comprising" and "modulation". As above, however, the claim amendments do not reflect a change in the scope of the invention for which protection is sought.

F. Claims 16 and 42 have been amended to remove the indefinite phrase "other psychiatric or clinical disfunctions [sic]". The Applicants expressly reserve the right to pursue claims to this subject matter in an application claiming the benefit of the filing date of the instant application. 35 USC § 120.

Accordingly, the Applicants respectfully request the withdrawal of the claim rejections based on 35 U.S.C. § 112¶2.

Claim Rejections Based on 35 USC § 112¶1

Claims 1-18 and 27-44 stand rejected under 35 U.S.C. § 112¶1 based on the Examiner's contention that the Specification does not enable any person skilled in the art to which it pertains or with which it is most nearly connected to make and use the invention commensurate in scope with the claims. Specifically, the Examiner contends that the Specification is enabling only for the exemplified compounds for inhibition of the reuptake of norepinephrine and epinephrine, thereby rendering the compounds useful for the treatment of depression, cocaine addiction and other maladies. The Applicants respectfully traverse this rejection.

Initially, the Applicants wish to express their sincere appreciation of the Examiner's evenhandedness in acknowledging that the level of skill in the monoamine art is high.

The Applicants acknowledge that no compound has been disclosed that is attached to a solid support, polymer, or biomolecule. Accordingly, the Applicants have amended claims 1, 7, 11, 27, 33, and 37 to remove every instance of those terms in a Markush group.

The Applicants respectfully contend that given the high level of skill in the monoamine art, the amended claims are adequately enabled, notwithstanding the fact that Figure 3 discloses the synthesis of only a limited number of compounds, because the level of skill in the art of synthetic organic chemistry is also high. Specifically, the Applicants respectfully assert that the level of ordinary skill in the art of synthetic organic chemistry is at least a PhD. Consequently, the Applicants respectfully contend that armed with the exemplification provided in the instant application and the teachings in the scientific literature pertaining to synthetic organic chemistry, one of ordinary skill in the art of synthetic organic chemistry would be able without undue experimentation to prepare compounds commensurate in scope with the claimed compounds.

Finally, with respect to amended claims 11-18 and 37-44, the Applicants respectfully assert that the Specification establishes that the compounds disclosed inhibit the reuptake of monoamines, which inhibition would render them effective in treating a disorder caused by a deficiency in the concentration of a monoamine. *See* claims 11 and

37; and Specification pp. 29-30. Further, the Applicants believe that the claim amendments removing "solid support, polymer and biomolecule" from the Markush groups defining the substitutents on the compounds used in the methods has decreased the scope of the claims to the point that it is commensurate with the enablement provided by the Applicants. In other words, the Applicants respectfully contend that due to the decreased scope of claims 11-18 and 37-44, the Specification would enable one of ordinary skill in the art to make and use the claimed invention without undue experimentation.

Accordingly, the Applicants respectfully request the withdrawal of the claim rejections based on 35 U.S.C. § 112¶1.

Conclusion

In view of the above amendments and remarks, the Applicants believe that the pending claims are in condition for allowance. If a telephone conversation with Applicants' Attorney would expedite prosecution of the application, the Examiner is urged to contact the undersigned. A marked-up version of the amended claims follows.

Respectfully submitted,
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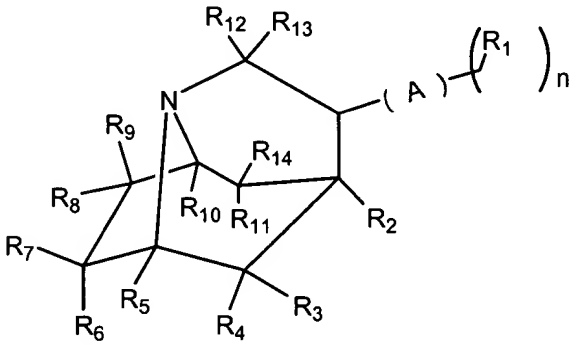
Date: 2/3/03

Marked-Up Version of Amended Claims Showing Changes Made

1. **(amended)** A [composition of] compound represented by formula **(I):**



(I)

wherein,

A is either a double bond or a single bond, n is 2 or 3, and each occurrence of R_1 is independently [comprises a moiety] selected from the group consisting of hydrogen, aryl, heteroaryl, cycloalkyl, polycyclic, heterocyclic, alkenyl, and alkynyl [, solid support unit, polymer, and biomolecule];

R_2-R_{13} each independently are [comprise a moiety] selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, polycyclic, heterocyclic, alkoxy, acyl, amino, hydroxy, thio, halogen, cyano, nitro, trifluoromethyl, azido, imino, amido, phosphoryl, sulfonyl, silyl group, ether, alkylthio, and carbonyl [, solid support unit, polymer, and biomolecule];

R_{14} [comprises a functionality] is selected from the group consisting of ester [moiety], O-R_{15}, wherein R_{15} is selected from the group consisting of alkyl, cycloalkyl, aryl, heteroaryl, alkenyl, and alkynyl; ketone; oxime; carboxylic acid; aldehyde; phosphoryl; and silyl; [solid support unit; polymer and biomolecule,] or a pharmaceutically acceptable salt thereof.

2. **(amended)** The [composition] compound of claim 1, wherein one occurrence of R_1 [comprises a moiety] is selected from the group consisting of aryl, heteroaryl, cycloalkyl, polycyclic, heterocyclic, alkenyl, and alkynyl; A is a double bond; n = 2; at least one occurrence of R_1 is hydrogen, and the compound is [whereby either] an E (entgegen) or Z (zusammen) isomer [is formed]; R_2-R_{13} each independently [comprise] represent hydrogen or alkyl; and R_{14} [comprises] is an ester [moiety].

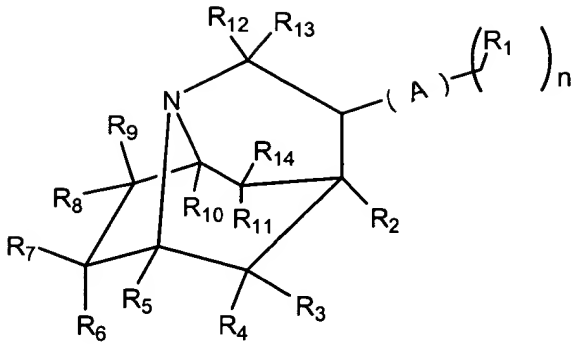
3. **(amended)** The [composition] compound of claim 1, wherein one occurrence of R_1 [comprises a moiety] is selected from the group consisting of haloaryl, alkoxy, alkylaryl, polycyclyl, alkenylaryl, and alkynylaryl; and either one or two occurrences of R_1 [comprise] represent hydrogen.

4. **(amended)** The [composition] compound of claim 1, wherein A is a double bond; n = 2; and one occurrence of R_1 is selected from the group consisting of phenyl, 3,4-Dichloro-phenyl, 4-methoxy-phenyl, 4-fluoro-phenyl, 1-napthyl, 2-furyl, 3-furyl, methoxy, and substituted or unsubstituted alkenylaryl, and the second occurrence of R_1 is hydrogen, and the compound is [whereby] an E (entgegen) isomer [is generated].

5. **(amended)** The compound of claim 1 [A selective norepinephrine and serotonin reuptake inhibitor (SSNRI) having the formula **(I)**], wherein one occurrence of R_1 [comprises] is 4-methoxy-phenyl, one occurrence of R_1 [comprises] is hydrogen; R_2-R_{13} each [comprise] represent hydrogen; and R_{14} [comprises] represents an ester [moiety].

6. **(amended)** The compound of claim 1 [A selective norephinephrine reuptake inhibitor (SNRI) having the formula **(I)**], wherein one occurrence of R_1 [comprises] is phenyl, one occurrence of R_1 [comprises] is hydrogen, R_2-R_{13} each [comprise] represent hydrogen, and R_{14} [comprises] represents an ester [moiety].

7. **(amended)** A pharmaceutical composition comprising a compound of formula **(I)**:



(I)

wherein,

A is either a double bond or a single bond, n is 2 or 3, and each occurrence of R_1 is independently [comprises a moiety] selected from the group consisting of hydrogen, aryl, heteroaryl, cycloalkyl, polycyclic, heterocyclic, alkenyl, and alkynyl [, solid support unit, polymer, and biomolecule];

R_2-R_{13} each independently are [comprise a moiety] selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, polycyclic, heterocyclic, alkoxy, acyl, amino, hydroxy, thio, halogen, cyano, nitro, trifluoromethyl, azido, imino, amido, phosphoryl, sulfonyl, silyl group, ether, alkylthio, and carbonyl [, solid support unit, polymer, and biomolecule];

R_{14} [comprises a functionality] is selected from the group consisting of ester [moiety], O-R_{15}, wherein R_{15} is selected from the group consisting of alkyl, cycloalkyl, aryl, heteroaryl, alkenyl, and alkynyl; ketone; oxime; carboxylic acid; aldehyde; phosphoryl; and silyl; [solid support unit; polymer and biomolecule,] or a pharmaceutically acceptable salt thereof; and

a pharmaceutically acceptable carrier.

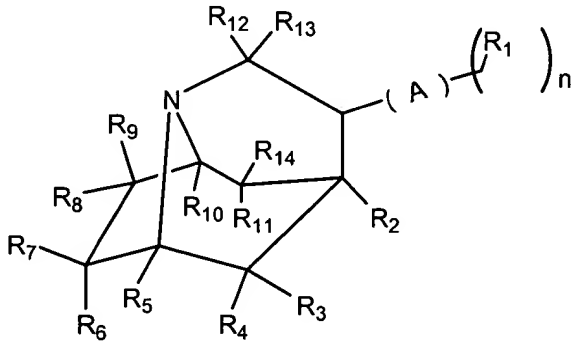
8. **(amended)** The pharmaceutical composition of claim 7, wherein one occurrence of R_1 [comprises a moiety] is selected from the group consisting of aryl, heteroaryl, cycloalkyl, polycyclic, heterocyclic, alkenyl, and alkynyl; A is a double bond; n = 2; at least one occurrence of R_1 is hydrogen, and the compound is [whereby either] an E (entgegen) or Z (zusammen) isomer [is formed]; and R_2-

R_{13} each independently [comprise] represent hydrogen or alkyl; and R_{14} [comprises] is an ester [moiety].

9. **(amended)** The pharmaceutical composition of claim 7, wherein one occurrence of R_1 [comprises a moiety] is selected from the group consisting of haloaryl, alkoxy, alkylaryl, polycyclyl, alkenylaryl, and alkynylaryl; and [either] one or two occurrences of R_1 [comprise] represent hydrogen.

10. **(amended)** The pharmaceutical composition of claim 7, wherein A is a double bond; n = 2; and one occurrence of R_1 is selected from the group consisting of phenyl, 3,4-Dichloro-phenyl, 4-methoxy-phenyl, 4-fluoro-phenyl, 1-napthyl, 2-furyl, 3-furyl, methoxy, and substituted or unsubstituted alkenylaryl, and the second occurrence of R_1 is hydrogen, and the compound is [whereby] an E (entgegen) isomer [is generated].

11. **(amended)** A method for treating a disorder[s] caused by a deficiency in monoamine concentration in a human [by] comprising administering a [pharmaceutically] therapeutically effective dose of a compound of formula **(I)**:



(I)

wherein,

A is either a double bond or a single bond, n is 2 or 3, and each occurrence of R_1 is independently [comprises a moiety] selected from the group consisting of hydrogen, aryl, heteroaryl, cycloalkyl, polycyclic, heterocyclic, alkenyl, and alkynyl [, solid support unit, polymer, and biomolecule];

R_2-R_{13} each independently [comprise a moiety] are selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, polycyclic, heterocyclic, alkoxy, acyl, amino, hydroxy, thio, halogen, cyano, nitro, trifluoromethyl, azido, imino, amido, phosphoryl, sulfonyl, silyl group, ether, alkylthio, and carbonyl [, solid support unit, polymer, and biomolecule];

R_{14} [comprises a functionality] is selected from the group consisting of ester [moiety], O-R_{15}, wherein R_{15} is selected from the group consisting of alkyl, cycloalkyl, aryl, heteroaryl, alkenyl, and alkynyl; ketone; oxime; carboxylic acid; aldehyde; phosphoryl; and silyl; [solid support unit; polymer and biomolecule,] or a pharmaceutically acceptable salt thereof.

12. **(amended)** The method of claim 11, wherein one occurrence of R_1 [comprises a moiety] is selected from the group consisting of aryl, heteroaryl, cycloalkyl, polycyclic, heterocyclic, alkenyl, and alkynyl; A is a double bond; n = 2; at least one occurrence of R_1 is hydrogen, and the compound is [whereby either] an E (entgegen) or Z (zusammen) isomer [is formed]; and R_2-R_{13} each independently [comprise] represent hydrogen or alkyl; and R_{14} [comprises] is an ester [moiety].

13. **(amended)** The method of claim 11, wherein one occurrence of R_1 [comprises a moiety] is selected from the group consisting of haloaryl, alkoxy, alkylaryl, polycyclyl, alkenylaryl, and alkynylaryl; and [either] one or two occurrences of R_1 [comprise] represent hydrogen.

14. **(amended)** The method of claim 11, wherein A is a double bond; n = 2; and one occurrence of R_1 is selected from the group consisting of phenyl, 3,4-Dichloro-phenyl, 4-methoxy-phenyl, 4-fluoro-phenyl, 1-napthyl, 2-furyl, 3-furyl, methoxy, and substituted or unsubstituted alkenylaryl, and the second occurrence of R_1 is hydrogen, and the compound is [whereby] an E (entgegen) isomer [is generated].

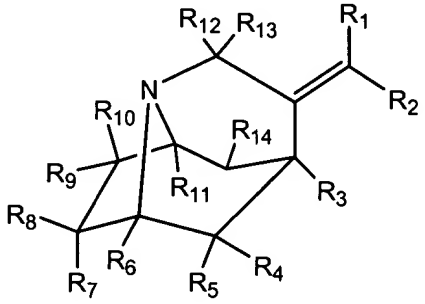
15. **(amended)** The method of claim 11, wherein said [disease or condition in a mammal comprises a disease or condition in a mammal in which] disorder in a human is associated with a deficiency in the [activity] concentration of serotonin or norepinephrine [is implicated and modulation of serotonin activity or serotonin or norepinephrine reuptake is desired].

16. **(amended)** The method of claim 11, wherein said [disease or condition in a mammal] disorder in a human is selected from the group consisting of depression, substance addiction, neurodegenerative disease, Attention Deficit Disorder, Huntington[s]'s Disease, and bipolar disorder [and other psychiatric or clinical disfunctions].

17. **(amended)** The method of claim 16, wherein said [neurodegenerative disease] disorder in a human is Parkinson's Disease or Alzheimer's Disease.

18. **(amended)** The method of claim 16, wherein said substance addiction [comprises] is cocaine addiction.

27. **(amended)** A [composition of] compound represented by formula **(II):**



(II)

wherein,

R_1 and R_2 each independently [comprise a moiety] are selected from the group consisting of hydrogen, aryl, heteroaryl, cycloalkyl, polycyclic, heterocyclic, alkenyl, and alkynyl [, solid support unit, polymer, and biomolecule];

R_3-R_{13} each independently [comprise a moiety] are selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, polycyclic, heterocyclic, alkoxy, acyl, amino, hydroxy, thio, halogen, cyano, nitro, trifluoromethyl, azido, imino, amido, phosphoryl, sulfonyl, silyl group, ether, alkylthio, and carbonyl [, solid support unit, polymer, and biomolecule];

R_{14} [comprises a functionality] is selected from the group consisting of ester [moiety], O-R_{15}, wherein R_{15} is selected from the group consisting of alkyl, cycloalkyl, aryl, heteroaryl, alkenyl, and alkynyl; ketone; oxime; carboxylic acid; aldehyde; phosphoryl; and silyl; [solid support unit; polymer and biomolecule,] or a pharmaceutically acceptable salt thereof.

28. **(amended)** The [composition] compound of claim 27, wherein [either] R_1 [or R_2 comprises a moiety] is selected from the group consisting of aryl, heteroaryl, cycloalkyl, polycyclic, heterocyclic, alkenyl, and alkynyl, and [either R_1 or] R_2 [comprises] is hydrogen, or R_2 is selected from the group consisting of aryl, heteroaryl, cycloalkyl, polycyclic, heterocyclic, alkenyl, and alkynyl, and R_1 is hydrogen, [whereby either] and the compound is an E (entgegen) or Z (zusammen) isomer [is formed]; R_3-R_{13} each independently [comprise] represent hydrogen or alkyl; and R_{14} [comprises] is an ester [moiety].

29. **(amended)** The [composition] compound of claim 27, wherein [either] R_1 [or R_2 comprises a moiety] is selected from the group consisting of haloaryl, alkoxy, alkylaryl, polycyclyl, alkenylaryl, and alkynylaryl; and [either R_1 or] R_2 [comprises] is hydrogen; or R_2 is selected from the group consisting of haloaryl, alkoxy, alkylaryl, polycyclyl, alkenylaryl, and alkynylaryl; and R_1 is hydrogen.

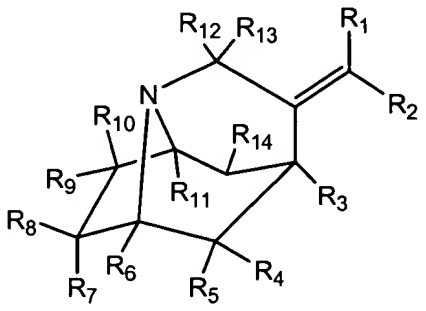
30. **(amended)** The [composition] compound of claim 27, wherein R_1 is selected from the group consisting of phenyl, 3,4-Dichloro-phenyl, 4-methoxy-phenyl, 4-fluoro-phenyl, 1-napthyl, 2-furyl, 3-furyl, methoxy, and substituted or unsubstituted alkenylaryl; and R_2 is hydrogen, [whereby] and the compound is an E (entgegen) isomer [is generated].

31. **(amended)** The compound of claim 27 [A selective norephinephrine and serotonin reuptake inhibitor (SSNRI) having the formula **(II)**], wherein R_1 [comprises] is 4-methoxy-phenyl, R_2 [comprises] is hydrogen, R_3-R_{13} each [comprise] represent hydrogen, and R_{14} [comprises] is an ester [moiety].

32. **(amended)** The compound of claim 27 [A selective norephinephrine reuptake inhibitor (SNRI) having the formula **(II)**], wherein R_1 [comprises] is phenyl, R_2

[comprises] is hydrogen, R_3-R_{13} each [comprise] represent hydrogen, and R_{14} [comprises] is an ester [moiety].

33. (**amended**) A pharmaceutical composition comprising a compound of formula **(II):**



(II)

wherein,

R_1 and R_2 each independently [comprise a moiety] are selected from the group consisting of hydrogen, aryl, heteroaryl, cycloalkyl, polycyclic, heterocyclic, alkenyl, and alkynyl [, solid support unit, polymer, and biomolecule];

R_3-R_{13} each independently [comprise a moiety] are selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, polycyclic, heterocyclic, alkoxy, acyl, amino, hydroxy, thio, halogen, cyano, nitro, trifluoromethyl, azido, imino, amido, phosphoryl, sulfonyl, silyl group, ether, alkylthio, and carbonyl [, solid support unit, polymer, and biomolecule];

R_{14} [comprises a functionality] is selected from the group consisting of ester [moiety], O-R_{15}, wherein R_{15} is selected from the group consisting of alkyl, cycloalkyl, aryl, heteroaryl, alkenyl, and alkynyl; ketone; oxime; carboxylic acid; aldehyde; phosphoryl; and silyl; [solid support unit; polymer and biomolecule,] or a pharmaceutically acceptable salt thereof; and

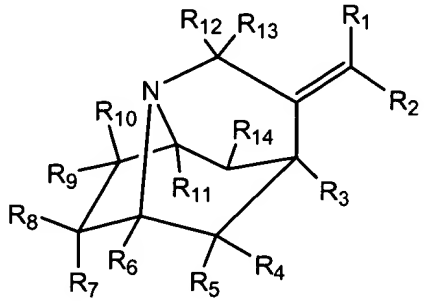
a pharmaceutically acceptable carrier.

34. (**amended**) The pharmaceutical composition of claim 33, wherein [either] R_1 [or R_2 comprises a moiety] is selected from the group consisting of aryl, heteroaryl, cycloalkyl, polycyclic, heterocyclic, alkenyl, and alkynyl, and [either R_1 or] R_2 [comprises] is hydrogen, or R_2 is selected from the group consisting of aryl, heteroaryl, cycloalkyl, polycyclic, heterocyclic, alkenyl, and alkynyl, and R_1 is hydrogen, [whereby either] and the compound is an E (entgegen) or Z (zusammen) isomer [is formed]; R_3-R_{13} each independently [comprise] represent hydrogen or alkyl; and R_{14} [comprises] is an ester [moiety].

35. (**amended**) The pharmaceutical composition of claim 33, wherein [either] R_1 [or R_2 comprises a moiety] is selected from the group consisting of haloaryl, alkoxy, alkylaryl, polycyclyl, alkenylaryl, and alkynylaryl; and [either R_1 or] R_2 [comprises] is hydrogen; or R_2 is selected from the group consisting of haloaryl, alkoxy, alkylaryl, polycyclyl, alkenylaryl, and alkynylaryl; and R_1 is hydrogen.

36. (**amended**) The pharmaceutical composition of claim 33, wherein R_1 is selected from the group consisting of phenyl, 3,4-Dichloro-phenyl, 4-methoxy-phenyl, 4-fluoro-phenyl, 1-napthyl, 2-furyl, 3-furyl, methoxy, and substituted or unsubstituted alkenylaryl; and R_2 is hydrogen, [whereby] and the compound is an E (entgegen) isomer [is generated].

37. (**amended**) A method for treating a disorder[s] caused by a deficiency in monoamine concentration in a human [by] comprising administering a [pharmaceutically] therapeutically effective dose of a compound of formula **(II)**:



(II)

wherein,

R_1 and R_2 each independently [comprise a moiety] are selected from the group consisting of hydrogen, aryl, heteroaryl, cycloalkyl, polycyclic, heterocyclic, alkenyl, and alkynyl [, solid support unit, polymer, and biomolecule];

R_3-R_{13} each independently [comprise a moiety] are selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, polycyclic, heterocyclic, alkoxy, acyl, amino, hydroxy, thio, halogen, cyano, nitro, trifluoromethyl, azido, imino, amido, phosphoryl, sulfonyl, silyl group, ether, alkylthio, and carbonyl [, solid support unit, polymer, and biomolecule];

R_{14} [comprises a functionality] is selected from the group consisting of ester [moiety], O-R_{15}, wherein R_{15} is selected from the group consisting of alkyl, cycloalkyl, aryl, heteroaryl, alkenyl, and alkynyl; ketone; oxime; carboxylic acid; aldehyde; phosphoryl; and silyl; [solid support unit; polymer and biomolecule,] or a pharmaceutically acceptable salt thereof.

38. **(amended)** The method of claim 37, wherein [either] R_1 [or R_2 comprises a moiety] is selected from the group consisting of aryl, heteroaryl, cycloalkyl, polycyclic, heterocyclic, alkenyl, and alkynyl, and [either R_1 or] R_2 [comprises] is hydrogen, or R_2 is selected from the group consisting of aryl, heteroaryl, cycloalkyl, polycyclic, heterocyclic, alkenyl, and alkynyl, and R_1 is hydrogen, [whereby either] and the compound is an E (entgegen) or Z (zusammen) isomer [is formed]; R_3-R_{13} each independently [comprise] represent hydrogen or alkyl; and R_{14} [comprises] is an ester [moiety].

39. **(amended)** The method of claim 37, wherein either R_1 [or R_2 comprises a moiety] is selected from the group consisting of haloaryl, alkoxy, alkylaryl, polycyclyl, alkenylaryl, and alkynylaryl; and [either R_1 or] R_2 [comprises] is hydrogen; or R_2 is selected from the group consisting of haloaryl, alkoxy, alkylaryl, polycyclyl, alkenylaryl, and alkynylaryl; and R_1 is hydrogen.

40. **(amended)** The method of claim 37, wherein R_1 is selected from the group consisting of phenyl, 3,4-Dichloro-phenyl, 4-methoxy-phenyl, 4-fluoro-phenyl, 1-

napthyl, 2-furyl, 3-furyl, methoxy, and substituted or unsubstituted alkenylaryl; and R_2 is hydrogen, [whereby] and the compound is an E (entgegen) isomer [is generated].

41. (**amended**) The method of claim 37, wherein said [disease or condition in a mammal comprises a disease or condition in a mammal in which] disorder in a human is associated with a deficiency in the [activity] concentration of serotonin or norepinephrine [is implicated and modulation of serotonin activity or serotonin or norepinephrine reuptake is desired].

42. (**amended**) The method of claim 37, wherein said [disease or condition in a mammal] disorder in a human is selected from the group consisting of depression, substance addiction, neurodegenerative disease, Attention Deficit Disorder, Huntington[s]'s Disease, and bipolar disorder [and other psychiatric or clinical disfunctions].

43. (**amended**) The method of claim 42, wherein said [neurodegenerative disease] disorder in a human is Parkinson's Disease or Alzheimer's Disease.

44. (**amended**) The method of claim 42, wherein said substance addiction [comprises] is cocaine addiction.